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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/583,335	02/15/2007	Shuxin Li	Q95559	9764

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EXAMINER
MURRAY, JEFFREY H

ART UNIT	PAPER NUMBER
1624	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/583,335	LI ET AL.	
	Examiner	Art Unit	
	Jeffrey H. Murray	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 June 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *3* is/are allowed.

6)☒ Claim(s) *1,2 and 4-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6/19/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. This action is in response to an application filed on July 19, 2006. There are twenty claims pending and twenty claims under consideration. This is the first action on the merits. The application concerns highly selective phosphodiesterase V inhibitors, pyrazolopyrimidinethione derivatives, and salts and solvates thereof, for preventing and/or treating impotence and frigidity, and their preparation methods and medical applications.

Priority

2. Acknowledgment is made of Applicant's claim for foreign priority. This application, U.S. Application No. 10/583,335, filed June 19, 2006, is a national stage application of PCT application PCT/CN04/01312, filed November 18, 2004, and claims foreign priority to Chinese Application No. 200310118481.8, filed December 18, 2003.

Specification

3. The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any of the errors of which applicant may become aware of in the specification.

Claim Rejections - 35 USC § 112, 1st

4. Claims 6 and 19 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a compound, composition or pharmaceutically acceptable salt, does not reasonably provide enablement for the solvate. The specification does not enable any person skilled in the art to

which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

5. The test of enablement is whether one skilled in the art could make and use the claimed invention from the disclosures in the application coupled with information known in the art without undue experimentation. (*United States v. Teletronics* Inc., 8 USPQ2d 1217 (Fed. Cir. 1988)). Whether undue experimentation is needed is not based on a single factor, but rather a conclusion reached by weighing many factors (See *Ex parte Forman* 230 USPQ 546 (Bd. Pat. App. & Inter. 1986) and *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988). These factors include the following:

1) *Amount of guidance provided by Applicant.* Applicant has provided no guidance, examples, or provided data and/or testing results of any solvates in the current application.

2) Unpredictability in the art. Predicting the formation of solvates or hydrates of a compound and the number of molecules of water or solvent incorporated into the crystal lattice of a compound is complex and difficult. Each solid compound responds uniquely to the possible formation of solvates or hydrates and hence generalizations cannot be made for a series of related compounds. Certain molecular shapes and features favor the formation of crystals without solvent; these compounds tend to be stabilized by efficient packing of molecules in the crystal lattice, whereas other crystal forms are more stable in the presence of water and/or solvents. There may be too many possibilities so that no computer programs are currently available for predicting

the crystal structures of hydrates and solvates. (*Advanced Drug Delivery Reviews*; **48**, (2001) 3-26.)

3) *Number of working examples.* Applicant has provided no working examples of a solvate in the present application.

4) *Nature of the invention.* The nature of this invention relates to a high selective phosphodiesterase V inhibitor, pyrazolopyrimidinethione derivatives, and salts and solvates thereof, for preventing and/or treating impotence and frigidity, and their preparation and medicinal applications.

5) *Level of skill in the art.* The artisan using Applicants invention would be a chemist with a Ph.D. degree, and having several years of bench experience.

MPEP §2164.01 (a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here that Applicant is not enabled for making these compounds or compositions.

6. Claims 13-19 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating impotence, does not reasonably provide enablement for the prevention impotence, nor the treating or prevention of frigidity. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

7. The test of enablement is whether one skilled in the art could make and use the claimed invention from the disclosures in the application coupled with information known in the art without undue experimentation. (*United States v. Teletronics* Inc., 8 USPQ2d 1217 (Fed. Cir. 1988)). Whether undue experimentation is needed is not based on a single factor, but rather a conclusion reached by weighing many factors (See *Ex parte Forman* 230 USPQ 546 (Bd. Pat. App. & Inter. 1986) and *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988). These factors include the following:

1) *Amount of guidance provided by Applicant.* Applicant has shown guidance as to these compounds having a "treating effect" on impotence according to the tables in the specification. Applicant, however, has shown no test results nor provided any biological or clinical data that suggests frigidity can be treated, in addition to being "prevented". In addition, all testing has taken place in rats, with the exception of testing the compound's effects on the heart in dogs. No explanation has been made or suggested as to why a positive test result in a male rat will definitely yield a positive test result within a human male.

2) Unpredictability in the art. The use of the term "prevention" is, unless otherwise defined, interpreted to mean inhibition of impotence or frigidity, once the active agent has been administered. Applicant must show that the claimed method "prevents impotence and frigidity in a broad range of conditions. The specification fails to enable the claimed compounds for the prevention of impotence or frigidity. The term "prevention" encompasses the ability of the specific antigen to induce protective immunity to any impotence and frigidity

disorders. In view of the situation set forth herein, it is clear that it is not possible for the instant compounds or compositions to "prevent" impotence and frigidity commensurate in scope with Claims 13-19.

The specification does not provide sufficient data or provide substantive evidence that the claimed compounds are capable of inducing protective immunity against impotence and frigidity disorders broadly. Without this demonstration, the skilled artisan would not be able to reasonably predict the outcome of the administration of the claimed compound, i.e. would not be able to accurately predict if an impotence or frigidity disorder had been prophlaxed.

3) *Number of working examples.* Applicant has provided no working examples of a compound or composition that has a "protective immunity" to any impotence or frigidity disorder in the present application.

4) *Nature of the invention.* The nature of this invention relates to a high selective phosphodiesterase V inhibitor, pyrazolopyrimidinethione derivatives, and salts and solvates thereof, for preventing and/or treating impotence and frigidity, and their preparation and medicinal applications.

5) *Level of skill in the art.* The artisan using Applicants invention would be a chemist with a M.S. or Ph.D. degree, and having several years of bench experience.

MPEP §2164.01 (a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention

without undue experimentation. *In re Wright*, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here that applicant is not enabled to treat or prevent frigidity and also unable to prevent impotence.

Claim Rejections - 35 USC § 112, 2nd

1. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 13-20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 13-20 recites the limitation "pharmaceutical" in the beginning of the claims. There is insufficient antecedent basis for this limitation in the claims.

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.

3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

10. Claims 1, 2, 4, and 5 are rejected under 35 U.S.C. 103(a) as being unpatentable over Baoshun et. al. (WO 2003016313) in view of Graver Tank & Mfg. Co. v. The Linde Air Products Co., (USSC 1950) 339 US 695, 85 USPQ 328. The current application recites a variety of specific novel substituted pyrazolopyrimidinethione compounds and compositions that can be used as phosphodiesterase V inhibitors. These compounds all contain a pyrazolo-pyrimidinethione core with various substitutents.

Baoshun et. al., teaches a group of compounds which are similar in scope to the current application. Within Baoshun et. al., the same core structure is present with one difference. The core of Baoshun et. al. is a pyrazolo-pyrimidinone, which contains a carbonyl group in the 4-position, whereas the present invention teaches a thione in the 4-position. Both the current application and Baoshun et. al. are being used as a treatment for impotence.

The court decision of Graver Tank & Mfg. Co. v. The Linde Air Products Co., (USSC 1950) 339 US 695, 85 USPQ 328 teaches that the important factor in determining a test for equivalency in a prior art document is whether a person who is reasonably skilled in the art would recognize the equivalency.

Relating the information from Graver Tank & Mfg. Co. v. The Linde Air Products Co., (USSC 1950) 339 US 695, 85 USPQ 328 to Baoshun et. al. publication, it would have been obvious for a person of ordinary skill in the art to try replacing the carbonyl derivative in the 4-position with a thione derivative in

the same position. Sulfur and oxygen are well known in the chemical arts to have similar properties. For example, both elements fall within the same family in the periodic table of the chemical elements. As atoms, both oxygen and sulfur contain the same valence number, similar chemical properties and numerous chemical literature has suggested the attempted use of a thiol over an alcohol or a thiourea in place of a urea and vice versa. Due to the numerous chemical property similarities of oxygen and sulfur, this substitution would be attempted by anyone skilled in the art.

The claims above are obvious because the substitution of one known element for another (sulfur for oxygen) would have yielded predictable results to one of ordinary skill in the art at the time of the invention.

Double Patenting

11. Applicant is advised that should claim 13, 15, or 17 be found allowable, claim 14, 16, 18, or 19 will be objected to respectively under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Allowable Subject Matter

12. Claim 3 is allowed.

13. The following is a statement of reasons for the indication of allowable subject matter: Claim 3 covers compounds not previously found or disclosed in

the prior art. The closest prior art to claim 3 is Kim, et. al. (WO 2002102802) which shows similar pyrazolopyrimidinethione compounds, however these compounds lack the required R^4 group required by the current application.

Conclusion

9. Claims 1, 2, and 4-20 are rejected.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey H. Murray whose telephone number is (571) 272-9023. The examiner can normally be reached on Mon-Thurs. 7:30-6pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. James O. Wilson can be reached at 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a US PTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

JHM

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